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(54) Title: METHODS OF MODULATING INFLAMMATORY REACTIONS BY MODULATING XANTHINE OXIDOREDUCTASE ACTIVITY

(57) Abstract: Evidence is presented that inflammation and injury involves activation of xanthine oxidoreductase (XOR) in the newly recruited mononuclear phagocytes (MNP). XOR has been shown to be increased predominantly in the MNP that increase rapidly in the lungs of rats that develop acute lung injury (ALI) following intratracheal cytokine insufflation. XOR was recovered from the MNP largely converted to its oxygen radical generating, reversible O-form, and alveolar MNP exhibited increased oxidative stress as evidenced by increased nitrotyrosine staining. Cytokine insufflation also increased alveolar cell apoptosis. A functional role for XOR in cytokine induced inflammation was demonstrated. Tungsten and allopurinol decreased MNP XOR induction, nitrotyrosine staining, inflammatory cell infiltration, and alveolar cell apoptosis. Transfer of control or allopurinol treated MNP into rat lungs, and confirmed a specific role for MNP XOR in promoting lung inflammation. These data indicate that XOR can contribute to lung inflammation by its expression and conversion in a highly mobile inflammatory cell population.



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